

Claims

1. A pharmaceutical composition comprising:

- 5 i) a safe and therapeutically effective amount of (1*S*, *cis*)-4-[2-amino-6-(cyclopropylamino)-9*H*-purin-9-yl]-2-cyclopentene-1-methanol or a pharmaceutically acceptable derivative thereof;
- ii) a safe and therapeutically effective amount of (2*R,cis*)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1*H*)-pyrimidin-2-one or a pharmaceutically acceptable derivative thereof; and
- iii) a pharmaceutically acceptable highly compressible carrier.

10 2. A pharmaceutical composition comprising:

- i) a safe and therapeutically effective amount of (1*S*, *cis*)-4-[2-amino-6-(cyclopropylamino)-9*H*-purin-9-yl]-2-cyclopentene-1-methanol or a pharmaceutically acceptable derivative thereof;
- 15 ii) a safe and therapeutically effective amount of (2*R,cis*)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1*H*)-pyrimidin-2-one or a pharmaceutically acceptable derivative thereof; and
- iii) a pharmaceutically acceptable highly compressible carrier

wherein said composition has a volume in the range of 1.0 - 1.3 mL.

3. A pharmaceutical composition in tablet form comprising:

- 20 i) a safe and therapeutically effective amount of (1*S*, *cis*)-4-[2-amino-6-(cyclopropylamino)-9*H*-purin-9-yl]-2-cyclopentene-1-methanol or a pharmaceutically acceptable derivative thereof;

- ii) a safe and therapeutically effective amount of (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one or a pharmaceutically acceptable derivative thereof; and
- iii) a pharmaceutically acceptable highly compressible carrier

5 wherein said composition exhibits a tablet hardness of greater than 18 kilopounds at 25 kilonewtons of force.

4. A pharmaceutical composition according to any of Claims 1- 3, wherein the pharmaceutically acceptable highly compressible carrier is selected from a group consisting of diluents, binders, and fillers.

10 5. A pharmaceutical composition according to Claim 4 wherein the pharmaceutically acceptable highly compressible binder is selected from the group consisting of highly compressible microcrystalline cellulose.

6. A pharmaceutical composition according to Claim 5 wherein the compressible microcrystalline cellulose is Ceolus® microcrystalline cellulose.

15 7. A pharmaceutical composition according to any of claims 1 - 3 comprising (1S, *cis*)-4-[2-amino-6-(cyclopropylamino)-9*H*-purin-9-yl]-2-cyclopentene-1-methanol, or a pharmaceutically acceptable derivative thereof, (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one, or a pharmaceutically acceptable derivative thereof, wherein said (1S, *cis*)-4-[2-amino-6-(cyclopropylamino)-9*H*-purin-9-yl]-2-cyclopentene-1-methanol and (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one are present in an amount of 20% to 80% of total composition weight.

20 8. A pharmaceutical composition according to any of Claims 1 - 7 wherein the amount of (1S, *cis*)-4-[2-amino-6-(cyclopropylamino)-9*H*-purin-9-yl]-2-cyclopentene-1-methanol is from about 15 to about 1200 mg per unit dosage form.

9. A pharmaceutical composition according to any one of Claims 1 - 7 wherein the amount of (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one is from about 15 to about 1500 mg per unit dosage form.
10. A pharmaceutical composition according to Claim 9 wherein the amount of (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one is from about 100 to about 500 mg per unit dosage form.
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11. A pharmaceutical composition according to Claim 10 wherein the amount of (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one is 300 mg per unit dosage form.
- 10 12. The pharmaceutical composition according to any of Claims 1 - 11 wherein (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one is provided substantially free of the corresponding (+)-enantiomer.
13. The pharmaceutical composition according to any of Claims 1 - 11 wherein (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one is provided such that the corresponding (+)-enantiomer is present in an amount of not more than about 5% w/w of the amount of lamivudine.
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14. The pharmaceutical composition according to any of Claims 1 - 8 wherein the pharmaceutically acceptable derivative of (1S, *cis*)-4-[2-amino-6-(cyclopropylamino)-9*H*-purin-9-yl]-2-cyclopentene-1-methanol is the hemisulfate salt.
- 20 15. The pharmaceutical composition according to any of Claims 1 - 6 wherein the pharmaceutically acceptable highly compressible carrier is present in an amount of 5% to about 50% by weight.
16. A pharmaceutical composition comprising (1S, *cis*)-4-[2-amino-6-(cyclopropylamino)-9*H*-purin-9-yl]-2-cyclopentene-1-methanol, or a pharmaceutically acceptable derivative thereof, (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one, and Ceolus[®] microcrystalline cellulose.
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17. A pharmaceutical composition consisting essentially of (1*S*, *cis*)-4-[2-amino-6-(cyclopropylamino)-9*H*-purin-9-yl]-2-cyclopentene-1-methanol, or a pharmaceutically acceptable derivative thereof, (2*R,cis*)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1*H*)-pyrimidin-2-one, and Ceolus® microcrystalline cellulose.
- 5 18. A pharmaceutical composition according to Claims 16 or 17 wherein the pharmaceutically acceptable derivative of (1*S*, *cis*)-4-[2-amino-6-(cyclopropylamino)-9*H*-purin-9-yl]-2-cyclopentene-1-methanol is the hemisulfate salt.
19. A pharmaceutical composition according to any of Claims 3 - 18 wherein the composition has a volume in the range of 1.0 - 1.3 mL.
- 10 20. A pharmaceutical composition according to any of Claims 1 - 19 in the form of a tablet.
21. A pharmaceutical composition according to any of Claims 1 - 20 for once daily administration.
- 15 22. A pharmaceutical composition according to any one of Claims 1 to 20 wherein the composition is coated with a pharmaceutically acceptable coating.
23. A method for maintaining high drug loading of a pharmaceutical composition by including a safe and effective amount of a pharmaceutically acceptable highly compressible carrier.
- 20 24. A method according to claim 23 wherein the highly compressible carrier is highly compressible microcrystalline cellulose.
25. A method for treating, reversing, reducing or inhibiting retroviral infections by administering a safe and effective amount of a composition according to any of Claims 1 - 21.

26. The method for treating, reversing, reducing or inhibiting retroviral infections according to Claim 25, wherein the retrovirus is HIV.

27. The use of (1*S*, *cis*)-4-[2-amino-6-(cyclopropylamino)-9*H*-purin-9-yl]-2-cyclopentene-1-methanol or a pharmaceutically acceptable derivative thereof, (2*R,cis*)-

5 4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1*H*)-pyrimidin-2-one or a pharmaceutically acceptable derivative thereof, and a pharmaceutically acceptable highly compressible carrier in the manufacture of a medicament of the treatment of a retroviral infection.

28. An article of manufacture comprising:

10 i) packaging material; and

ii) a pharmaceutical composition contained within the packaging material, comprising:

a) a safe and therapeutically effective amount of (1*S*, *cis*)-4-[2-amino-6-(cyclopropylamino)-9*H*-purin-9-yl]-2-cyclopentene-1-methanol or a pharmaceutically acceptable derivative thereof;

15 b) a safe and therapeutically effective amount of , (2*R,cis*)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1*H*)-pyrimidin-2-one or a pharmaceutically acceptable derivative thereof; and

c) a pharmaceutically acceptable highly compressible carrier

20 wherein friability, hardness and disintegration of the resulting composition is maintained.

29. An article of manufacture according to Claim 28 additionally comprising a brochure containing product information.

30. An article of manufacture according to Claim 28 or Claim 29 wherein the packaging material is unit dose blister packaging.

31. A process for the preparation of a pharmaceutical composition as claimed in any of claims 1-13 which process comprises admixture of (1*S*, *cis*)-4-[2-amino-6-(cyclopropylamino)-9*H*-purin-9-yl]-2-cyclopentene-1-methanol or a pharmaceutically acceptable derivative thereof, , (2*R,cis*)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1*H*)-pyrimidin-2-one or a pharmaceutically acceptable derivative thereof, and a pharmaceutically acceptable highly compressible carrier.